

We claim

1. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes
a protein comprising the amino acid sequence as set forth in **Figure 11, 13, or 19.**

2. An isolated nucleic acid molecule which encodes MAFBX, or a fragment thereof,
having a sequence selected from the group consisting of

a) the nucleotide sequence comprising the coding region of MAFBX as set
forth in Figure 10, 12, or 19;

(b) a nucleotide sequence who complement hybridizes under stringent
conditions to the nucleotide sequences of (a) and which encodes a molecule having
the biological activity of MAFBX; or

(c) a nucleotide sequence which, but for the degeneracy of the genetic code
would hybridize to a complement of the nucleotide sequence of (a) or the
complement of (b), and which encodes a molecule having the biological activity of
MAFBX.

3. An isolated nucleic acid molecule which is derived from a mammalian genome
that:

a) hybridizes under stringent conditions to the nucleic acid molecule of
Figures 10, 12, or 18; and

b) encodes a gene product which contains a ring domain

4. An isolated polypeptide encoded by the nucleic acid molecule of claim 1, 2, or 3.

5. A vector which comprises a nucleic acid molecule of claim 1, 2, or 3.

6. A vector according to claim 5, wherein the nucleic acid molecule is operatively
linked to an expression control sequence capable of directing its expression in a host
cell.

7. A host-vector system for the production of MAFBX polypeptide which comprises
a host cell transformed with the vector of claim 5.

8. A host-vector system according to claim 7 wherein the host cell is a bacterial, yeast, insect or mammalian cell.

9. A transgenic animal having cells which harbor a transgene comprising the nucleic acid of Claims 1,2,or 3.

10. An animal inactivated in the loci comprising the nucleotide sequence of claims 1,2,or 3.

11. An antibody which binds the MAFBX polypeptide of claim 4.

12. A MAFBX antagonist for use in a method of inhibiting atrophy, inducing hypertrophy, decreasing ubiquitination, interfering with the ubiquitin pathway, or modulating MAFBX expression or activity.

13. An antagonist of the MAFBX pathway for use in a method of inhibiting atrophy, inducing hypertrophy, decreasing ubiquitination, interfering with the ubiquitin pathway, or modulating MAFBX expression or activity.

14. A method of screening compounds useful for the treatment of muscle atrophy or detecting atrophy and related diseases and disorders comprising contacting a muscle cell expressing MAFBX with a compound and detecting a change in the MAFBX protein activity or ubiquitination.

15. The method of claim 14 wherein the change is measured by PCR, Taqman PCR, phage display systems, gel electrophoresis, yeast-two hybrid assay, Northern or Western analysis, immunohistochemistry, a conventional scintillation camera, a gamma camera, a rectilinear scanner, a PET scanner, a SPECT scanner, a MRI scanner, a NMR scanner, or an X-ray machine.

16. The method of claim 14 where in the change in the MAFBX protein activity is detected by detecting a change in the interaction of the MAFBX with one or more proteins, or by detecting a change in the level of ubiquitination of one or more of the proteins in the ubiquitin pathway.

17. The method of claim 14 in which one of the one or more proteins is the substrate

of MAFBX.

18. The method of claim 14 wherein the muscle cell is of skeletal muscle origin.

5 19. The method of claim 14 wherein the muscle cells are cultured cells.

20. The method of claim 14 wherein the muscle cells are obtained from a transgenic organism.

10 21. The method of claim 20 wherein the transgenic organism includes, but is not limited to a mouse, rat, rabbit, sheep, cow or primate.

22. The method of claim 14 wherein the muscle cells are within a transgenic organism.

23. The method of claim 22 wherein the transgenic organism includes, but is not limited to a mouse, rat, rabbit, sheep, cow or primate.

20 24. The method of claim 14 wherein the MAFBX and the molecule capable of detecting MAFBX are nucleic acids.

25 25. The method of claim 14 wherein the MAFBX and the molecule capable of detecting MAFBX are polypeptides.

26. The method of claim 14 wherein the compound is a substrate for MAFBX.

27. The method of claim 14 wherein the change in protein expression is demonstrated by a change in amount of protein of one or more of the proteins in the ubiquitin pathway.

30 28. A method of detecting muscle atrophy in an animal comprising measuring MAFBX in a patient sample.

35 29. A method of inhibiting atrophy or inducing hypertrophy by modulating MAFBX or an F-box thereof.

30. A method of treating illnesses, syndromes or disorders associated with muscle

atrophy comprising administering to an animal a compound that modulates the MAFBX pathway, ubiquitination, the expression or activity of MAFBX or the F-box of MAFBX such that symptoms are alleviated.

- 5 31. The method of claim 30 such that the animal is a mammal.
32. The method of claim 30 such that the mammal is a human

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